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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|----------------------------|------------------|
| 09/721,414 | 11/22/2000 | Hiroaki Suga | 11520.0222 | 2737 |
| 7590 | 05/19/2004 | | | |
| Ranjana Kadle Hodgson Russ Andrews Woods & Goodyear LLP One M&T Plaza Suite 2000 Buffalo, NY 14203-2391 | | | EXAMINER SCHULTZ, JAMES | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1635 | |
| DATE MAILED: 05/19/2004 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/721,414

Applicant(s)

SUGA ET AL.

Examiner

J. Douglas Schultz

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003 and 03 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7 and 13-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7 and 13-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 402020 3/22/04
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date here with
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of Amendments and Claims

1. The originally filed claims were subject to a restriction mailed October 6, 2003, due to the presence of multiple sequences which, at the time, was considered to give rise to multiple inventions. In response to the restriction requirement applicants amended the claims in a manner that was considered to be non-compliant because more than one sequence remained in the amended claims. A notice of non-compliance was mailed to applicants on January 28, 2004 to this effect. Applicants responded by electing Group 65. However, following a conversation with applicants' representative John Lopinski, It was agreed that both the notice of non-compliance set forth in the action mailed January 28, 2004, and applicants election of Group 65 in the response dated March 3, 2004 would be vacated, and the amended claims submitted November 10, 2003 would be examined, because the two remaining sequences recited in the amended claims are used together in the same method and are not a burden to search. Accordingly, the first Official action on the merits is provided below, and is directed to the claims submitted November 10, 2003.

2. The amended claims submitted November 10, 2003 incorrectly identify claim 7 as "original", when in fact, the preamble has been changed from "A method of identifying" to "A method for constructing", and should thus read "amended".

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and by dependency claims 13-16, recite the limitation "partitioning the aminoacylated ribozyme". There is insufficient antecedent basis for "the aminoacylated ribozyme" in the claim, as there is no absolute requirement that any ribozymes are aminoacylated in the previous steps, particularly in view of the specification's teachings that this method is essentially a random screening procedure that suggests there may be instances where no ribozymes are ever aminoacylated. Replacing the phrase containing these words with "partitioning aminoacylated RNA molecules from non-aminoacylated RNA molecules wherein the aminoacylated RNA molecules are cis-aminoacylating catalytic RNA molecules aminoacylated with the amino acid substrate", as recited in claim 17, would obviate this rejection.

4. Claim 17, and by dependency claims 18-20, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites a method for constructing cis-aminoacylating catalytic RNA molecules. However, the method steps indicate that an RNA molecule is already provided having a tRNA-like domain and a 5' leader ribozyme. Thus it appears that the molecule is already constructed, and cannot be properly considered a method for constructing said molecules, because the method steps test whether any of the already-constructed molecules contain any inherent ability to become cis-aminoacylated. Clarification is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 14-17, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The subject matter of the instantly claimed invention is drawn to a method for constructing cis-aminoacylating catalytic RNA molecules comprising the steps of attaching a tRNA-like molecule and a ribozyme domain molecule via the 5' end of the tRNA-like molecule to obtain a pool of ribozyme-tRNA molecules, and contacting the ribozyme-tRNA molecules with an amino acid substrate, and isolating any aminoacylated ribozyme-tRNA molecules.

At the outset it is noted that the rejected claims do not recite any specific sequence referring to "tRNA-like". Said sequences are thus considered to be claimed by the broad function of being tRNA-like, rather than by any particular or specific structure. While the specification discloses that tRNA-like means "RNA molecules that have sequences consistent with the formation of a cloverleaf structure typically associated with tRNAs", it is maintained that one of skill could not predict *a priori* whether an RNA sequence will form secondary structures from a mere knowledge of the sequence as discussed further below, and accordingly, cannot be given much patentable consideration. In the absence of a clear definition in the specification, such language is considered extremely broad and is considered to embrace any RNA sequence that

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binds any amino acid according to the art accepted usage tRNA. Applicants are not considered to be in possession of such broad genus.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

While the specification defines tRNA-like as “RNA molecules that have sequences consistent with the formation of a cloverleaf structure typically associated with tRNAs”, such cloverleaf structures cannot be predicted *a priori*. As seen in the reference of Tinoco *et al.*, (J. Mol. Biol. (1999) 293, 271-281), one cannot use the primary structure of RNA alone to reliably predict the presence of secondary or tertiary structures, because experimental thermodynamic data is required. Even here, thermodynamic conditions can vary widely, and have dramatic

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impacts on the folding of RNA structures. Temperature and salt concentrations are integral aspects of the thermodynamic conditions that provide for and result in a given secondary structure as indicated in Tinoco. Thus, a single RNA sequence may have vastly different secondary structures depending on temperature and salt concentration. Finally, metal binding sites need to be determined and characterized, which is a process that also must be determined experimentally. It is thus maintained that one of skill could not use a reference to cloverleaf structures to envision the genus of tRNA-like sequences in the absence of any other information.

While the specification provides several examples of nucleic acid sequences that are aminoacylated and thus are "tRNA-like", there is no mention of whether these sequences are consistent with the formation of cloverleaf structures that are alleged to be typically associated with tRNAs. Moreover, this relatively small number of disclosed species is not considered representative of the genus of any tRNA-like molecule as broadly recited.

One of skill in the art could not immediately envision the genus of tRNA-like molecules from the disclosure of only a few tRNA-like molecules, particularly in view of the size and unpredictability of the genus as discussed above. A few sequences is not considered to provide adequate support for a genus of tRNA-like molecules that is both large and varied, because one of skill in the art would not be apprised as to what structural features actually define the genus of any tRNA-like molecule. Accordingly, applicants are not considered to be in possession of the genus of any tRNA-like molecules as claimed.

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Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Lohse *et al.*

(AW on applicants IDS; Nature, 1996. Vol. 381:442-4).

The invention of the instant claims is relied upon as discussed above.

Lohse *et al.* describe constructing a pool of RNA molecules, each containing a ribozyme along with both random and constant domains. Lohse *et al.* further describe introducing a 3' fragment of a charged tRNA molecule to said pool, and then enriching the fraction of the constructed RNA molecules that undergo cis-aminoacylation via utilization of the fragment tRNA as an amino acid donor.

Lohse *et al.* is considered to anticipate the instant claims because, as described above, the term “tRNA-like” is considered to be sufficiently broad enough that the teachings of Lohse *et al.* meet the claim limitations. While these same claims were rejected under 35 U.S.C. § 112 first paragraph written description because applicants were not considered to be in possession of the broad genus of any “tRNA-like” molecule, particularly given the broad definition provided in the specification “tRNA-like”, a reasonable, art-accepted interpretation of the term tRNA-like includes any RNA sequence that is shown to bind an amino acid. This is the interpretation relied upon below.

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Lohse teaches RNA constructs that contain a ribozyme at the 5' end of the construct (see bottom bridging paragraph of pg. 442) that are capable of catalyzing the addition of an amino acid residue onto itself (and are thus tRNA-like as discussed above). Thus, Lohse teaches attaching a ribozyme domain molecule to the 5' end of a tRNA-like molecule to obtain a pool of ribozyme-tRNA like molecules, contacting them with a substrate (the charged '3 tRNA fragment), and partitioning them based on their ability to cis-aminoacylate. Accordingly, Lohse *et al.* teaches all the limitations of the instant claims, and thus anticipates the instant invention.

7. Claims 7 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Suga *et al.* (AX on applicants IDS).

The invention of the instant claims is relied upon as discussed above.

Suga *et al.* describe constructing a pool of RNA molecules, each containing a ribozyme along with both random and constant domains. Suga *et al.* further describe introducing a 3' hexanucleotide molecule to said pool, and then enriching the fraction of the constructed RNA molecules that undergo cis-aminoacylation.

Suga teaches RNA constructs that contain a ribozyme at the 5' end of the construct that are capable of catalyzing the addition of an amino acid residue onto itself. Accordingly, Suga teaches attaching a ribozyme domain molecule to the 5' end of a tRNA-like molecule to obtain a pool of ribozyme-tRNA like molecules, contacting them with a substrate (the charged '3 tRNA fragment), and partitioning them based on their ability to cis-aminoacylate. Accordingly, Suga *et al.* teaches all the limitations of the instant claims, and thus anticipates the instant invention.

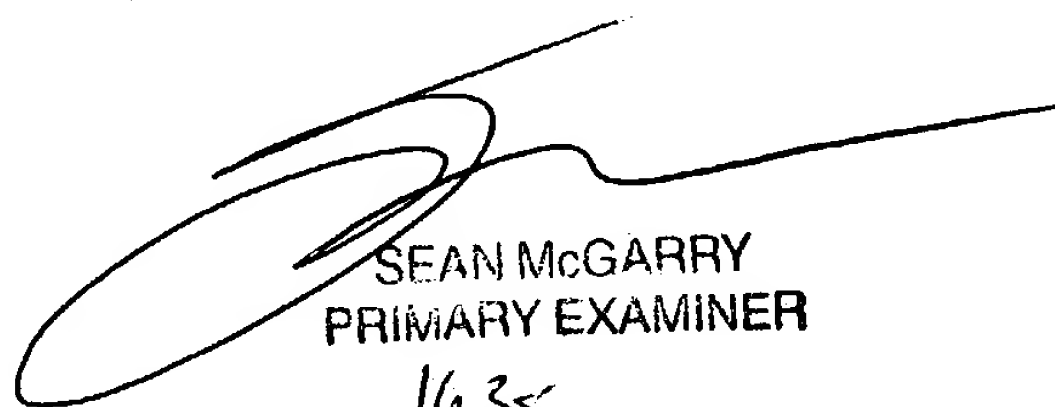
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Douglas Schultz, PhD



SEAN MCGARRY
PRIMARY EXAMINER
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